

**PLEASE AMEND THE CLAIMS AS FOLLOWS:** namely,

1. (Withdrawn) A pharmaceutical composition for neuraxial delivery comprising both a hydrophilic N-linked glycosyl prodrug compound and a formulary, wherein said hydrophilic N-linked glycosyl prodrug compound comprises a CNS acting prodrug compound covalently linked with a saccharide through an amide or an amine bond and said formulary comprises an agent selected from the group consisting of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, an emollient, a disintegrant, a lubricating agent, an antimicrobial agent and a preservative,

with the proviso that said saccharide moiety is not a cyclodextrin or a glucuronide.

2. (Withdrawn) The pharmaceutical composition of claim 1, further comprising a dosage form selected from the group consisting of a powder, a granule, an emollient cream, a tablet, a capsule, a lozenge, a trouch, a suppository, a perenteral solution, an injection solution, a syrup, an elixir, a nasal solution, a intrabronchial solution, an ophthalmic solution, a dermal patch and a bandage.

3. (Withdrawn) The pharmaceutical composition of claim 1, wherein said hydrophilic N-linked glycosyl prodrug compound further comprises a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises a CNS-acting prodrug compound; B, comprises a lower alkyl; D, comprises a nitrogen linker amine or amide; and, E comprises a saccharide, with the proviso that E is not a cyclodextrin or a glucuronide.

4. (Currently Amended) The pharmaceutical composition method of claim 41 wherein said A-moiety ~~comprises~~ is a CNS acting prodrug compound selected from the group consisting of a stimulant, an anti-depressant, a neurotransmitter, a dopaminergic agent, a metabolic precursor compound, a muscle relaxant, a tranquilizer, an analgesic, a narcotic, a sedative, a hypnotic, a narcotic antagonist, a narcotic analgesic, an anti-hypotensive agent, a  $\beta$ -blocker, an anti-hypertensive

agent, a vasodilator, an anesthetic, an anti-epileptic compound, an anti-convulsant drug, a hormone, a sympatholytic agent, a centrally acting anti-cholinergic compound, a sympathetic stimulant, an adrenergic agent, a barbiturate antagonist, an anti-infective agent, an anticholinergic agent, an anticonvulsant, a sympatholytic, an ACE inhibitor, an anti-epilepsy agent, an antiviral agent, a gonadotropin synthesis stimulant, a diuretic and an emetic agent.

5. (Currently Amended) The ~~pharmaceutical composition method~~ of claim [[41]] 4, wherein said CNS acting prodrug ~~further comprises is~~ a dopaminergic agonist or antagonist.

6. (Withdrawn) A process for preparing a hydrophilic N-linked glycosyl prodrug compound for neuraxial delivery, comprising the step of N-linking a CNS acting prodrug compound with a saccharide moiety under conditions suitable for formation of an amide or amine bond between said CNS acting prodrug compound and said saccharide moiety.

7. (Withdrawn) The process of claim 6, wherein said hydrophilic N-linked glycosyl prodrug compound comprises a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises said CNS-acting prodrug; B, comprises an optional lower alkyl; D, comprises said N-linker amine or amide; and, E comprises said saccharide, with the proviso that E is not a cyclodextrin or a glucuronide.

8. (Withdrawn) A process for preparing a pharmaceutical composition comprising hydrophilic N-linked glycosyl prodrug compound for neuraxial delivery, comprising the steps of N-linking a CNS acting prodrug compound with a saccharide moiety under conditions suitable for formation of an amide or amine bond between said CNS acting prodrug compound and said saccharide moiety; and formulating said N-linked glycosyl prodrug compound into said pharmaceutical composition by addition of an agent selected from the group consisting of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, an emollient, a disintegrant, a lubricating agent, an antimicrobial agent and a preservative.

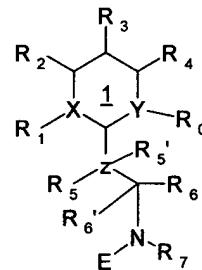
9. (Withdrawn) A method for treating a neurological dysfunction in a subject in need thereof comprising the step of administering to the subject a pharmaceutical composition comprising a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises a CNS-acting prodrug; B, comprises a lower alkyl; D, comprises a nitrogen linker amine or amide; and, E comprises a saccharide, with the proviso that E is not a cyclodextrin.

10. (Currently Amended) The method of claim 41, wherein said compound ~~further comprises~~ is a compound according to FORMULA IV,



Formula IV

wherein,

Ring 1 ~~comprises~~ is a cyclic or heterocyclic ring, or aryl or heteroaryl ring, all of said rings comprising 4 to 8 carbon atoms, among which atoms are counted "X" and "Y";

R<sub>0</sub>, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> ~~comprise~~ are substituents of Ring 1;

either of X or Y is optional; each of X and Y, when present ~~comprise~~ is a carbon atom, a halogen atom or a lower alkyl;

~~Z, R<sub>5</sub> and R<sub>6</sub> are optional; when Z is present it comprises a lower alkyl having substituents R<sub>5</sub>, R<sub>6</sub>;~~

~~R<sub>6</sub> and R<sub>6</sub> comprise substituents on a carbon atom linking Z with N through a single bond, or when Z is absent, linking N with Ring 1;~~

~~N comprises a nitrogen atom of an amine or an amide linked with E through a single bond and having R<sub>7</sub> as a substituent; and~~

E ~~comprises~~ is a saccharide;

with the proviso that when E is a monosaccharide it is not a C<sub>6</sub> glucuronic acid and when E is an oligosaccharide it is not a cyclodextrin.

11. (Currently Amended) The method of claim 10, wherein said Ring 1 ~~comprises~~ is an optionally substituted aryl or heteroaryl ring wherein if either one of X or Y comprises a halogen or oxygen and then the remaining other of X or Y comprises a carbon atom.

12. (Original) The method of claim 11, wherein said R<sub>2</sub> and R<sub>3</sub> are hydroxyl.

13. (Previously Presented) The method of claim 12, wherein said R<sub>1</sub> and R<sub>4</sub> are selected from the group consisting of hydrogen, hydroxyl, halogen, halo-lower alkyl, alkoxy, alkoxy-lower alkyl, halo-alkoxy, thioamido, amidosulfonyl, alkoxycarbonyl, carboxamide, amino-carbonyl and alkylamine-carbonyl.

14. (Currently Amended) The method of claim 10, wherein each of X and Y ~~comprise a lower is an alkyl chain~~ having 2 carbon atoms.

15. (Currently Amended) The method of claim 10, wherein each of X and Y ~~comprise a lower is an alkyl chain~~ having 1 carbon atom.

16. (Currently Amended) The method of claim 10, wherein Z ~~comprises a lower is an alkyl~~ having 1 or 2 carbon atoms.

17. (Original) The method of claim 16, wherein said R<sub>5</sub> and R<sub>5'</sub> are selected from the group consisting of hydrogen, hydroxyl, alkoxy, carboxyl, alkoxylcarbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl.

18. (Original) The method of claim 17, wherein said R<sub>6</sub> and R<sub>6'</sub> are selected from the group consisting of hydrogen, hydroxyl, alkoxy, carboxyl, alkoxylcarbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl.

19. (Currently Amended) The method of claim 10, wherein Z and R<sub>6</sub> comprise is a carbonyl group, N comprises an is a nitrogen atom of an amide and R<sub>7</sub> is hydrogen.

20. (Currently Amended) The method of claim 10, wherein R<sub>7</sub> comprises is a hydrogen and N comprises is a nitrogen atom of an amine.

21. (Original) The method of claim 10, wherein said E substituent is selected from the group consisting of a radical of a monosaccharide, a disaccharide, a trisaccharide and an oligosaccharide

22. (Currently Amended) The method of claim 10, wherein said E monosaccharide comprises is a radical of a sugar selected from the group consisting of aldose, ketoaldose, alditols, ketoses, aldonic acids, ketoaldonic acids, aldaric acids, ketoaldaric acids, amino sugars, keto-amino sugars, uronic acids, ketouronic acids, lactones and keto-lactones.

23. (Original) The method of claim 22, wherein said radical of a sugar is further selected from the group consisting of triosyl, tetraosyl, pentosyl, hexosyl, heptosyl, octosyl and nonosyl radicals and derivatives thereof.

24. (Currently Amended) The method of claim 23, wherein said pentosyl sugar radical comprises is a straight carbon chain<sub>1,2</sub> or a furanosyl ring or a derivative thereof.

25. (Currently Amended) The method of claim 23, wherein said hexosyl sugar radical comprises is a straight carbon chain, a furanosyl ring<sub>1,2</sub> or a pyranosyl ring or a derivative thereof.

26. (Original) The method of claim 23, wherein said hexosyl radical is further selected from the group consisting of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fructose, ribo-hexulose, arabino-hexulose<sub>1,2</sub> and lyxo-hexulose and derivatives thereof.

27. (Original) The method of claim 23, wherein said pentosyl radical is further selected from the group consisting of ribose, arabinose, xylose, lyxose, ribulose<sub>1,2</sub> and xylulose and derivatives thereof.

28. (Currently Amended) The method of claim 23, wherein said heptosyl residue ~~comprises~~ is sedoheptulose and derivatives thereof.

29. (Currently Amended) The method of claim 23, wherein said nonosyl residue ~~comprises~~ is N-acetylneuraminic acid, N-glycolylneuraminic acid[[],] and diacetylneuraminic acid, ~~and~~ derivatives thereof.

30. (Currently Amended) The method of claim 26, wherein said compound ~~further comprises~~ is glucose, galactose[[],] or fructose ~~or~~ derivatives thereof.

31. (Currently Amended) The method of claim 21, wherein said disaccharide, trisaccharide and oligosaccharide ~~comprise~~ is a sugar homopolymer or a sugar heteropolymer.

32. (Original) The method of claim 31, wherein said sugar homopolymer comprises a glycoside selected from the group consisting of erythran, threan, riban, arabinan, xylan, lyxan, allan, altran, glucan, mannan, gulan, idan, galactan, talan[[],] and fructan ~~and~~ derivatives thereof.

33. (Currently Amended) The method of claim 31, wherein said sugar heteropolymer ~~further comprises~~ is a glycoside selected from the group consisting of erythroside, threoside, riboside, arabinoside, xyloside, lyxoside, alloside, altroside, glucoside, mannoside, guloside, idoside, galactoside, taloside[[],] and fructoside ~~and~~ derivatives thereof.

34. (Currently Amended) The method of claim 33, wherein said sugar heteropolymer ~~further comprises~~ is a glycoside metabolized in a mammal to a glucosyl or a galactosyl monosaccharide.

35. (Currently Amended) The method of claim 32, wherein said glycoside ~~further comprises~~ is a riban, an arabinan, a glucan, a galactan[[],] and a mannan ~~and~~ derivatives thereof.

36. (Currently Amended) The method of claim 33, wherein said glycoside ~~further comprises~~ is a riboside, an arabinoside, a glucoside, a galactoside, a mannoside[[],] and a fructoside ~~and~~ derivatives thereof.

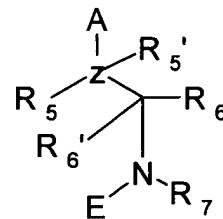
37. (Currently Amended) The method of claim 34, wherein said glucan ~~comprises~~ is maltose, amylose, glycogen, cellobiose, amylopectin[[],] and heparin and derivatives thereof.

38. (Currently Amended) The method of claim 35, wherein said glucoside ~~comprises~~ is sucrose and derivatives thereof.

39. (Currently Amended) The method of claim 35, wherein said fructoside ~~comprises~~ is fucosidolactose and derivatives thereof.

40. (Currently Amended) The method of claim 35, wherein said galactoside ~~comprises~~ is lactose, hyaluronic acid[[],] and pectin and derivatives thereof.

41. (Currently Amended) A method for improving the aqueous solubility and blood brain barrier penetrability of a drug, comprising the steps of forming [[a]] covalent ~~chemical bond~~ linkages between the drug, a bridging hydrocarbon moiety, a nitrogen atom of an amine or amide and a sugar or oligosaccharide, wherein the reaction product of said steps is said drug ~~comprises all of an A, a B and a D moiety, and said step of forming a covalent chemical bond between the drug and said sugar or oligosaccharide results in the formation of reaction product that is a compound according to~~ FORMULA I:



Formula I

wherein, each of "-" ~~comprises~~ is a single bond; A, ~~comprises~~ is a cyclic, heterocyclic, aryl or heteroaryl CNS-acting prodrug selected from TABLE A or from TABLE B; [B, comprises a bridging hydrocarbon moiety having one to six carbon atoms linked at two of said carbon atoms through

single bonds with each of A and D; D, comprises an amine or amide linked through single bonds with each of B and E; and,]

Z, R<sub>5</sub> and R<sub>5'</sub> are optional; when Z is present is a lower alkyl having substituents R<sub>5</sub>, R<sub>5'</sub>;  
R<sub>6</sub> and R<sub>6'</sub> are substituents on a carbon atom linking Z with N through a single bond, or when  
Z is absent, linking N with Ring 1;

N is a nitrogen atom of an amine or an amide linked with E through a single bond and having  
R<sub>7</sub> as a substituent; and

E comprises is a saccharide, with the proviso that when E is a monosaccharide it is not a C<sub>6</sub> glucuronic acid and when E is an oligosaccharide it is not a cyclodextrin.

42. (Withdrawn) A method of treating a subject in need thereof to effect a metabolic replacement therapy, comprising the step of administering to said subject a therapeutic compound, wherein said therapeutic compound comprises a hydrophilic compound transportable intact by an intestinal glucose transporter, transportable intact in blood, transportable intact by endothelial cells at a blood brain barrier and metabolizable by a neuronal cell, wherein said therapeutic compound further comprises a compound binding to a dopamine receptor and metabolizable in said neuronal cell to effect said metabolic replacement therapy and said subject comprises a patient with a neurological dysfunction, a Parkinson's disease or a Parkinson's related disease.